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Letter to the Editor

Letter to the editor, regarding "Iatrogenic cerebral amyloid angiopathy: Two case reports to explore clinical heterogeneity and pathological patterns" recently published by Vera-Cáceres and colleagues

Dear Editor,

Iatrogenic cerebral amyloid angiopathy (iCAA) is a rare but significant condition that can develop decades after neurosurgical interventions, particularly those involving cadaveric or bovine lyophilized dural transplants in early childhood.[1] The Queen Square (QSC) diagnostic criteria classify iCAA cases as probable or possible.[2]

We comment Vera-Cáceres and colleagues who presented two cases of probable iCAA with slow disease progression that deviates from the typical course.[3] While most iCAA cases involve recurrent intracerebral hemorrhages (ICH), poor prognosis, and mortality within months,[2,4] including our previously described case[5], these cases with chronic disease courses, recurrent events, and favorable functional recovery provide valuable insights into iCAA's clinical heterogeneity. This broadens our understanding of its variability.

We present a new case of iCAA with a chronic course, further supporting evidence of variability in iCAA progression.

A 43-year-old male presented to our department in December 2018 with acute left-sided hemiparesis. His history included a traumatic brain injury with a left occipitoparietal skull fracture, treated with lyophilized dura implantation at six months of age. His development and professional trajectory were unremarkable, with no family history of neurological disorders. On admission, he was alert and oriented with moderate dysarthria, left-sided central facial paresis, left tongue deviation, plegia of the left upper limb, and moderate paresis of the left lower limb (National Institutes of Health Stroke Scale (NIHSS) 9, modified Rankin Scale (mRS) 5). Non-contrast computed tomography (CT) revealed a right frontal cortico-subcortical ICH (3 × 3 cm) with perilesional edema (Fig. 1A) and cortical encephalomalacia in the left parietal lobe. Bone CT confirmed a prior craniectomy. CT angiography and laboratory tests, including coagulation profiles and tumor markers, were normal.

Transient worsening of edema with subfalcine herniation seen on follow up CT (Fig. 1B) was successfully treated conservatively with mannitol and dexamethasone. After six weeks of neurorehabilitation the patient had a residual left-sided hemiparesis and he was discharged with NIHSS 9 and mRS 4.

Magnetic resonance imaging (MRI) revealed cortical superficial siderosis (Fig. 1C). Cerebrospinal fluid (CSF) analysis revealed reduced amyloid-beta (Aβ)-42 levels (480 pg/mL), and genetic testing showed no hereditary CAA mutations. The patient was diagnosed with probable iCAA based on QSC criteria.

Over subsequent 6 years, he experienced two transient episodes of left-sided paresthesias. MRI follow-ups showed recurrent ICH and cortical subarachnoid hemorrhages (Fig. 1D–G). At his latest check-up in December 2024, his condition remained stable, with mild anomia, left-sided spastic hemiparesis (NIHSS 4, mRS 3) and no cognitive decline. Amyloid positron emission tomography imaging is still planned.

In conclusion, this case demonstrates a chronic iCAA course, consistent with the cases described by Vera-Cáceres et al.[3] Further studies on iCAA phenotypes are needed. Key questions remain: Can we identify iCAA patients likely to exhibit slower progression? Could biomarkers serve as predictive tools? What is the optimal follow-up interval for repeated brain imaging? To address these questions, using standardized diagnostic protocol and establishing a multinational registry would be crucial for advancing our understanding of this disease.

Patient consent statement

Informed consent was obtained from the patient's relative involved in the study. Written consent was obtained from the patient's relative for the publication of this case report and the accompanying figures, which are part of the patients' records archived by the hospital.

Ethics approval

The present research complies with the guidelines for human studies, and the research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Data availability statement

No data are available.

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CRediT authorship contribution statement

Matija Zupan: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Janja Pretnar Oblak:** Conceptualization, Writing – original draft, Writing – review & editing. **Senta Frol:** Conceptualization, Data curation, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

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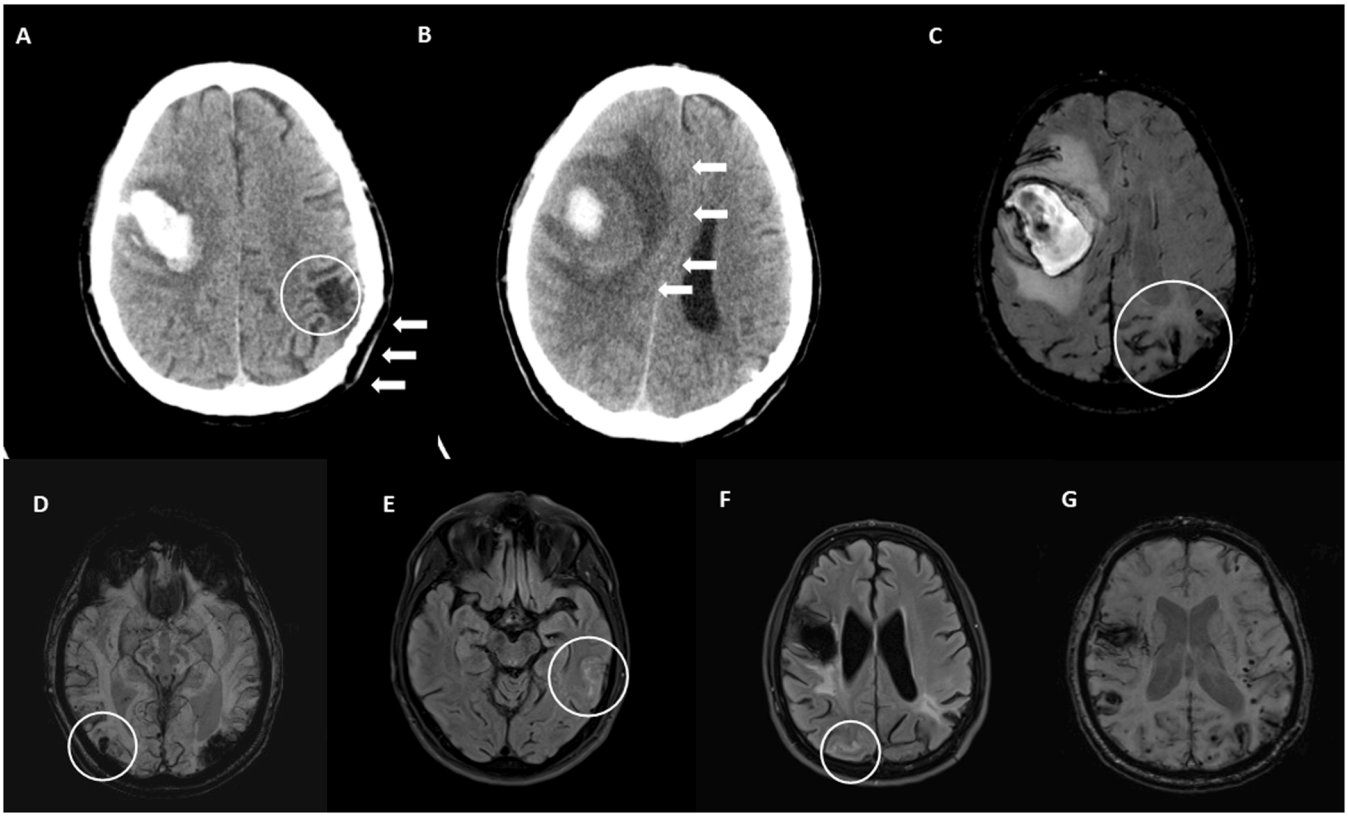

Fig. 1. A. A non-contrast CT (NCCT) on admission showing a hyperdense (fresh) intracerebral hematoma (ICH) in the right frontal lobe with perilesional edema and an encephalomalatic tissue in the left parietal lobe, over which post-craniectomy signs can be seen (arrows). B. A NCCT 10 days post-admission showing a substantial enlargement of the perilesional edema causing a subfalcine herniation to the left (arrows). C. A susceptibility—weighted (SWI) MRI 14 days post-admission showing a subacute ICH in the right fronto-parietal region, without any clear signs of a tumor, and a substantial perilesional edema; a hypointensive cortical superficial siderosis (CSS) pronounced over the left parietal lobe is seen (circle). D. An SWI MRI in November 2021 showing a small recent cortico-subcortical ICH in the right occipital lobe (circle). E. A fluid-attenuated inversion recovery (FLAIR) MRI in February 2024 showing a hyperintensive (acute) cortical subarachnoid hemorrhage (SAH) in the sulci of the left temporal lobe (circle). F. A FLAIR MRI in September 2024 showing a hyperintensive (acute) cortical SAH over the right parietal lobe. G. An SWI MRI in September 2024 showing multiple hypointensive microhemorrhages in the left cerebral hemisphere and an extensive CSS over both cerebral hemispheres.

the work reported in this paper.

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